

DETAILED ACTION

1. Applicant's amendment and response filed 6/9/11 is acknowledged and has been entered.

2. Applicant is reminded of Applicant's election of Group II without traverse in Applicant's response filed 12/7/09 and Applicant's election without traverse of the species env for both immunogen and antigen, MIP-1 α , HIV as the condition to be treated and GM-CSF as the adjuvant in Applicant's response filed 9/30/10.

Claims 1, 5, 7-9, 12, 15-16, 19 and 40-43 read on the elected species.

Applicant is reminded that upon consideration of the prior art, examination has been extended to include the species recited in instant claim 17.

Applicant is reminded that base claim 1 contains limitations that belong to non-elected groups, *i.e.*, at part "(ii)".

Claims 1, 5, 7-9, 12, 15-17, 19 and 40-43 are currently being examined as they read on the administration of polypeptides.

Note that claims 41-43 are listed as rejected on the Office Action summary mailed 12/9/10.

3. Applicant's amendment filed 6/9/11 has overcome the prior rejection of claims 27 and 28 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

4. Applicant's amendment filed 6/9/11 has overcome the prior rejection of claims 20-22 and 25-28 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before

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November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

6. Claims 1, 5, 7-9, 12, 15-17, 19, 40 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 02/36141 (Applicant's IDS reference filed 7/20/11).

This is a new ground of rejection necessitated by Applicant's IDS filed 7/20/11.

WO 02/36141 teaches administering a combination of from two to five agents from the following: those that mobilize dendritic cells, stimulate maturation of dendritic cells, enhance an immune response of an effector T cell, or agents that cause death or growth inhibition of infectious agents (especially abstract). WO 02/36141 teaches that induction of cell mediated immune response requires the interaction of at least three different types of cells: DC, CD4+ Th cells and CD8+ effector T cells or CTL (especially page 1 at paragraph 3). WO 02/36141 teaches that an agent or more than one agent is administered to an individual human including an infant afflicted with or at risk for a condition characterized by the presence of a pathogenic or opportunistic organism(s), said agent being a DC mobilization factor such as human or murine FLT3L or a biologically active fragment thereof and/or GM-CSF, a chemoattractant(s) to attract the mobilized DC such as MIP-1 α and or MIP-3 α , along with one or more antigens, said antigens may be HIV antigens, other viral antigens, bacteria, yeast, fungi and protozoa or viruses that cause cancer or demyelinating autoimmune diseases. WO 02/36141 teaches that the various agents may be administered locally in or near a site of infection or systemically. WO 02/36141 teaches that the agents may be administered to humans in a variety of administration forms and dosages. WO 02/36141 teaches optionally administering a second anti-microbial or anti-viral therapy. WO 02/36141 teaches administering a second therapeutic regimen within 1 to 25 days after the first. WO 02/36141 teaches administration by such routes as SC, IV and IM. WO 02/36141 teaches that those of ordinary skill in the art are able to optimize the order and/or time of the steps as well as the dosages and routes of administration by routine experimentation (especially page 2 at the first two paragraphs, page 10 at paragraph 2, page 11 at paragraphs 1 and 3, page 18 at paragraphs 2 and 3, pages 20-23, claims, Figure 1, page 5 at paragraph 1, pages 6-9).

With regard to the inclusion of instant claims 7 and 8 in this rejection, although the art reference does not teach the % T cell response augmentation, the method steps taught by the art are the same method steps recited in the instant claim.

As per MPEP 2111.04, claim scope is not limited by claim language that suggests or makes optional but does not require steps to be performed, or by claim language that does not limit a claim to a particular structure. However, examples of claim language, although not exhaustive, that may raise a question as to the limiting effect of the language in a claim are:

(A) "adapted to" or "adapted for" clauses;

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(B) "wherein" clauses; and

(C) "whereby" clauses.

The determination of whether each of these clauses is a limitation in a claim depends on the specific facts of the case. In Hoffer v. Microsoft Corp., 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005), the court held that when a "'whereby' clause states a condition that is material to patentability, it cannot be ignored in order to change the substance of the invention." *Id.* However, the court noted (quoting Minton v. Nat'l Ass'n of Securities Dealers, Inc., 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003)) that a "'whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.'"

In the instant case, the recited "wherein" clause (claims 7 and 8) simply expresses the intended result that occurs upon performing the method steps.

7. Claims 1, 5, 7-9, 12, 15-17, 19 and 40-43 are rejected under 35 U.S.C. 102(e) as being anticipated by US 6,933,377 B2.

US 6,933,377 B2 discloses treating and preventing HIV by administering an HIV gene product(s) wherein the administering includes administering one or more adjuvants that is/are a co-stimulatory molecule, a cytokine, a chemokine and a growth factor. US 6,933,377 B2 discloses that these adjuvants may include Flt3 ligand, GM-CSF growth factor and chemokine MIP-1 α , and the route of administration is preferably IM, IV, IP and SC. US 6,933,377 B2 discloses that the env, pol and/or gag gene products are immunogens that can be used in the method. US 6,933,377 B2 further discloses that the administering may be to a neonate, a child, an adolescent or an adult human, nonhuman primate, cow, horse, sheep, rodent, goat or cat, and that the providing step may be one administration or multiple administrations. US 6,933,377 B2 discloses that the immune response may be a CTL and/or Th response (*i.e.*, a CD8+ T cell and/or CD4+ T cell response, respectively). US 6,933,377 B2 discloses that the providing can be performed using a single formulation or at least two separate formulations, including wherein the formulations are by the same route of administration such as by IM, SC or IV administration (especially abstract, column 1 at lines 55-67, column 2 at lines 1-29 and 55-59, column 3 at lines 19-23, Tables 1 and 2, column 16 at lines 64-67, column 17 at lines 1-10, column 20 at lines 65-67, column 21 at lines 1, 40-49).

With regard to the inclusion of instant claims 7 and 8 in this rejection, although the art reference does not teach the % T cell response augmentation, the method steps taught by the art are the same method steps recited in the instant claim.

As per MPEP 2111.04, claim scope is not limited by claim language that suggests or makes optional but does not require steps to be performed, or by claim language that does not limit a claim to a particular structure. However, examples of claim language,

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although not exhaustive, that may raise a question as to the limiting effect of the language in a claim are:

- (A) "adapted to" or "adapted for" clauses;
- (B) "wherein" clauses; and
- (C) "whereby" clauses.

The determination of whether each of these clauses is a limitation in a claim depends on the specific facts of the case. In Hoffer v. Microsoft Corp., 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005), the court held that when a "'whereby' clause states a condition that is material to patentability, it cannot be ignored in order to change the substance of the invention." *Id.* However, the court noted (quoting Minton v. Nat'l Ass'n of Securities Dealers, Inc., 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003)) that a "'whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.'"

In the instant case, the recited "wherein" clause (claims 7 and 8) simply expresses the intended result that occurs upon performing the method steps.

Applicants arguments have been fully considered but are not persuasive.

Applicant's arguments are of record in the amendment and response filed 6/9/11 on pages 10-12.

However, the method of the instant claims recites "said method comprising providing", thus opening the claim to administration of additional components besides the immunogen, Flt3L and MIP-1 α . In addition, the art reference discloses prophylactic and therapeutic vaccination using a composition comprising the immunogen and at least one molecular adjuvant, two of which are disclosed to be MIP-1 α and Flt3L. Thus, Applicant's argument that the genus of adjuvants and combinations thereof includes hundreds or thousands of possible combinations and that only a very small number of these combinations would include the claimed combination and the skilled artisan could not at once envisage the particular combination of Flt3L and MIP-1 α amongst all possible combinations is not persuasive.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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9. Claims 1, 5, 7-9, 12, 15-17, 19 and 40-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/09303 (Applicant's IDS reference filed 7/20/11).

This is a new ground of rejection necessitated by Applicant's IDS filed 7/20/11.

WO 01/09303 teaches enhancing an immune response to an immunogen comprising administering a composition encoding one or more immunogens, Flt-3L (including human or murine) or active fragment thereof, and at least one cytokine such as MIP-1 α by such routes as IV, IM, ID or SC. WO 01/09303 also teaches that co-injection of mouse Flt-3L and poorly immunogenic antigen(s) can influence the quality of the immune response to said antigen(s) to produce an increase in the B- and T-cell responses. WO 01/09303 teaches that the immunogenic composition to be administered can also contain a polynucleotide that encodes GM-CSF. WO 01/09303 teaches that determining the number and timing of doses are within the ordinary skill in the art and will be readily determined by the attending physician or veterinarian (especially first full paragraph on page 2, paragraph spanning pages 2-3, paragraph spanning pages 14-15, page 16 at the first full paragraph, page 17 at the first paragraph, paragraph spanning pages 17-18, first two paragraphs on page 18, page 29, page 30 at lines 1-11, page 39 at the first full paragraph, claims).

WO 01/09303 does not teach that the method of enhancing an immune response comprises administering a composition comprising protein constituents rather than the polynucleotide(s) encoding the immunogen(s), Flt3-L, MIP-1 α and optionally GM-CSF.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have administered the components of the polynucleotide containing composition taught by the art reference as proteins rather than polynucleotides encoding the proteins in the art method of enhancing an immune response.

One of ordinary skill in the art would have been motivated to do this because the art reference teaches that Flt-3L and antigen(s) protein administration is effective, and it would have been obvious to use any effective form of composition in the art method.

Alternatively, WO 01/09303 does not teach that the method of coinjecting the protein antigen(s) and Flt3-L in order to stimulate an immune response also includes coinjecting MIP-1 α and optionally GM-CSF.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have included MIP-1 α and optionally GM-CSF in the protein composition in the method for stimulating an immune response taught by the art reference.

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One of ordinary skill in the art would have been motivated to do this because the art reference teaches including polynucleotides encoding MIP-1 α and optionally GM-CSF in the polynucleotide composition of the art method.

With regard to the inclusion of instant claims 7 and 8 in this rejection, although the art reference does not teach the % T cell response augmentation, the method steps taught by the art are the same method steps recited in the instant claim.

As per MPEP 2111.04, claim scope is not limited by claim language that suggests or makes optional but does not require steps to be performed, or by claim language that does not limit a claim to a particular structure. However, examples of claim language, although not exhaustive, that may raise a question as to the limiting effect of the language in a claim are:

- (A) "adapted to" or "adapted for" clauses;
- (B) "wherein" clauses; and
- (C) "whereby" clauses.

The determination of whether each of these clauses is a limitation in a claim depends on the specific facts of the case. In Hoffer v. Microsoft Corp., 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005), the court held that when a "'whereby' clause states a condition that is material to patentability, it cannot be ignored in order to change the substance of the invention." *Id.* However, the court noted (quoting Minton v. Nat'l Ass'n of Securities Dealers, Inc., 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003)) that a "'whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.'"

In the instant case, the recited "wherein" clause (claims 7 and 8) simply expresses the intended result that occurs upon performing the method steps.

Claims 40-42 are included in this rejection because the art reference teaches that number and timing of doses is within the purview of one of ordinary skill in the art, and thus it would have been *prima facie* obvious to have determined an optimal dosing regimen using a single formulation versus at using at least two separate formulations, and including wherein said formulations are provided by the same route of administration.

10. Claims 1, 5, 7-9, 12, 15-17, 19 and 40-43 are rejected are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 02/36141 (Applicant's IDS reference filed 7/20/11).

This is a new ground of rejection necessitated by Applicant's IDS filed 7/20/11.

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WO 02/36141 teaches administering a combination of from two to five agents from the following: those that mobilize dendritic cells, stimulate maturation of dendritic cells, enhance an immune response of an effector T cell, or agents that cause death or growth inhibition of infectious agents (especially abstract). WO 02/36141 teaches that induction of cell mediated immune response requires the interaction of at least three different types of cells: DC, CD4+ Th cells and CD8+ effector T cells or CTL (especially page 1 at paragraph 3). WO 02/36141 teaches that an agent or more than one agent is administered to an individual human including an infant afflicted with or at risk for a condition characterized by the presence of a pathogenic or opportunistic organism(s), said agent being a DC mobilization factor such as human or murine FLT3L or a biologically active fragment thereof and/or GM-CSF, a chemoattractant(s) to attract the mobilized DC such as MIP-1 α and or MIP-3 α , along with one or more antigens, said antigens may be HIV antigens, other viral antigens, bacteria, yeast, fungi and protozoa or viruses that cause cancer or demyelinating autoimmune diseases. WO 02/36141 teaches that the various agents may be administered locally in or near a site of infection or systemically. WO 02/36141 teaches that the agents may be administered to humans in a variety of administration forms and dosages. WO 02/36141 teaches optionally administering a second anti-microbial or anti-viral therapy. WO 02/36141 teaches administering a second therapeutic regimen within 1 to 25 days after the first. WO 02/36141 teaches administration by such routes as SC, IV and IM. WO 02/36141 teaches that those of ordinary skill in the art are able to optimize the order and/or time of the steps as well as the dosages and routes of administration by routine experimentation (especially page 2 at the first two paragraphs, page 10 at paragraph 2, page 11 at paragraphs 1 and 3, page 18 at paragraphs 2 and 3, pages 20-23, claims, Figure 1, page 5 at paragraph 1, pages 6-9).

WO 02/36141 does not teach wherein the providing is performed using at least two separate formulations, and including provided by the same route of administration.

The art reference teaches that number and timing of doses is within the purview of one of ordinary skill in the art, and thus it would have been prima facie obvious to have determined an optimal dosing regimen using a single formulation versus at using at least two separate formulations, and including wherein said formulations are provided by the same route of administration.

With regard to the inclusion of instant claims 7 and 8 in this rejection, although the art reference does not teach the % T cell response augmentation, the method steps taught by the art are the same method steps recited in the instant claim.

As per MPEP 2111.04, claim scope is not limited by claim language that suggests or makes optional but does not require steps to be performed, or by claim language that does not limit a claim to a particular structure. However, examples of claim language, although not exhaustive, that may raise a question as to the limiting effect of the language in a claim are:

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The determination of whether each of these clauses is a limitation in a claim depends on the specific facts of the case. In Hoffer v. Microsoft Corp., 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005), the court held that when a "'whereby' clause states a condition that is material to patentability, it cannot be ignored in order to change the substance of the invention." *Id.* However, the court noted (quoting Minton v. Nat'l Ass'n of Securities Dealers, Inc., 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003)) that a "'whereby' clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited."

In the instant case, the recited "wherein" clause (claims 7 and 8) simply expresses the intended result that occurs upon performing the method steps.

11. No claim is allowed.

12. The reference crossed-out in Applicant's From 1449 filed 7/20/11 is not a complete citation.

13. Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 7/20/11 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Nickol, can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marianne DiBrino, Ph.D.
Patent Examiner
Group 1640
Technology Center 1600

/G. R. Ewoldt/
Primary Examiner, Art Unit 1644